UNITED STATES DEPARTMENT OF COMMERCE
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Washington, D.C. 20231

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
|---|---|---|---|
| 09/675,511 | 09/29/00 | WOLF | L 112754-019 |

| EXAMINER | |
|---|---|
| SAUCIER, S | |
| ART UNIT | PAPER NUMBER |
| 1651 | |

DATE MAILED: 07/30/01

HM22/0730

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

# Office Action Summary

| Application No. | Applicant(s) |
|---|---|
| 09/675,511 | Wolf Jr. et al. |
| **Examiner** | **Art Unit** |
| Sandra Sauci r | 1651 |

*-- Th MAILING DATE of this communication appears on th cover sh t with the c rrespond nc address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) ☐ Responsive to communication(s) filed on _____

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

**Disposition of Claims**

4) ☒ Claim(s) 28-39 is/are pending in the applica

4a) Of the above, claim(s) _____ is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 28-39 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

**Application Papers**

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 3

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

## DETAILED ACTION

Claims 28-39 are pending and are considered on the merits.

### *Claim Rejections - 35 USC § 112*

### INDEFINITE

Claims 28-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 28 is directed to inactivating viruses in "a body fluid". However, the specification defines "body fluid" as red cells, white cell, bone marrow, platelets (p. 6, l. 1-5), and even"internal organs" (p. 8, l. 10). Clearly, these materials are not "fluids" as defined by Webster's New World Dictionary [U]. Although the definition in the specification includes these non-fluid cells and organs, applicants cannot define a term in opposition to a generally accepted definition. In re Hill 73 USPQ 482 (CCPA 1970).

Claim 28 requires that the container that contains the blood fluid is made of PVC material. However, it also requires that an inner surface of the container be made of non-PVC plastic material. This appears to be a contradiction. If the container is made of PVC, it cannot have non-PVC materials.

It is unclear if the word "plastic" in claim 28, line 4 is meant to modify "polyvinyl chloride" or if the container is a plastic which is not a PVC type material. Are both containers made of plastic? If the punctuation in the claim was, non-PVC, plastic material, it might be interpreted to intend that both containers were made of any plastic, except PVC. In the absence of such punctuation, it is interpreted that only the inner surface is required to be something other than the plastic, PVC, but the container itself is not required to be plastic. If the container is made of a plastic, which is not PVC, some such simple English expression might be clearer.

The claims require that both containers have a non-PVC plastic inner surface. The specification explains how a PVC surface absorbs MB, while a non-PVC surface does not absorb MB. Therefore, the surface of the container of claim 28, according to the specification does not absorb MB. However, claim 37 requires that surface to absorb MB. The claims are not logical in light of the specification.

Claim 30 has no precedent for the recitation of "blood component". Please note that red cells, white cells and platelets, etc., are not body fluids.

Claim 31 in which the mixture is formed is required be made of plastic. However, PVC is a plastic and when the mixture is made in the body fluid container, the claim limitation does not further limit and even expands the independent claim. When the mixture is made in the MB container, the inner surface, at least, is also plastic. Therefore, this container, too, is at least in part made of plastic. The intent of this limitation is unclear.

Claim 33 requires that one of the two containers be PVC. However, the independent claim requires that the inner surface be non-PVC. If a container has a non-PVC material in it, it cannot be made of PVC.

Claim 35 appears to be redundant since the independent claim requires that both containers have a non-PVC inner surface. The mixing must occur in one of the two stipulated containers.

There may be new matter in the newly presented claims, but they are so garbled and do not follow logically from one to the other that the intent of the claims cannot be determined.

NEW MATTER

Claims 28-39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Insertion of the limitation "sterile, sealed containers, each container having an inner surface made of a non-polyvinyl chloride plastic material" has no support in the as-filed specification. The insertion of this limitation is a new concept because it neither has literal support in the as-filed specification by way of generic disclosure, nor is there a specific example of the new limitation which would show possession of the concept of the use of "*sterile, sealed* containers with inner surface made of a non-polyvinyl plastic material" for the storage of methylene blue or "sterile sealed containers with an inner surface made of a *non-polyvinyl plastic material*" for the storage of body fluids, as there is no exemplification contained in the specification. This is a matter of

written description, not a question of what one of skill in the art would or would not have known. The material within the four corners of the as-filed specification must lead to the concept. If it does not, the material is new matter. Declarations and new references cannot demonstrate the possession of a concept after the fact. Thus, the insertion of this phrase is considered to be the insertion of new matter for the above reasons.

Pointing to the passage where this limitation is recited with reference to both methylene blue and body fluid containers would overcome the rejection.

ENABLEMENT

Claims 28-39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

NATURE OF THE INVENTION

The invention is directed to the inactivation of viruses in a body fluid in a first container by mixing with methylene blue which is initially in a separate, second container and irradiation of the mixture. The claims are indefinite, but are interpreted to mean that the first container containing the body fluid and the second container containing the methylene blue have at least an inner lining which is not PVC.

BREADTH OF THE CLAIMS

The claims encompass the irradiation of any body fluid, which is defined to include material which is not a body fluid such as organs and cells after mixture with methylene blue. The claims are very confusing, but appear to have both the methylene blue and the body fluid in containers which are at least lined with a non-polyvinyl plastic material.

AMOUNT OF GUIDANCE AND WORKING EXAMPLES

The specification fails to describe the concentration of methylene blue that should be added to the body fluid in order to inactivate pathogens. Applicants admit on page 9, lines 1-5, the criticality of such concentrations, but fail to divulge such critical concentrations. Some guidance with regard to the concentrations of methylene blue is required, particularly with regard to the adsorption technique which is recited in a dependent claim. The specification

states on page 5, that "It has been found that methylene blue does not migrate into non-PVC material as **well** (bold mine) as into PVC material under sterilization conditions.". This statement implies that at least some methylene blue DOES migrate into non-PVC material. Thus, even in the embodiment where methylene blue is in a container which has a non-PVC inner surface, as claimed, at least some leaching is to be expected.

No guidance is provided with regard to the amounts of methylene blue which can be adsorbed by a blood or plasma bag, the time required for such an adsorption nor any other conditions are given such as temperature, surface area necessary, intensity, duration of exposure or any other parameter.

STATE OF THE PRIOR ART AND UNPREDICTABILITY

The prior art does not appear to have disclosed the absorption of methylene blue by plastic containers and thus, cannot be relied upon for guidance on the above parameters.

Further, the prior art reveals that unpredictability is associated with the irradiation of blood components with methylene blue in order to inactivate pathogens. Floyd [C8] disclose that photoactivation of methylene blue causes damage to lymphocytes (example 5 and column 3, line 20 onward). The claims broadly claim the use of the instant method for a body fluid. Body fluids and blood components may contain cells such as lymphocytes.

Judy *et al.* [C2] disclose the uncertainties associated with the proper irradiation of blood samples, especially samples containing erythrocytes (column 16, line 40).

Neyndorff *et al.* [D3] disclose that light penetration into the sample and intensity of the light has an effect on viral inactivation when using photoactive compounds.

Clearly the area of viral inactivation with photoactive dyes is unpredictable and the practice of the invention has not been supported by the specification because no guidance with regard to the concentration of methylene blue, time and intensity of irradiation, depth of sample or other parameters have been disclosed.

The disclosure is considered to be little more than an invitation to experiment.

In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of the enablement varies inversely with the degree of unpredictability of the factors involved. *Ex parte Humphreys*, 24 USPQ2d, 1260.

Undue experimentation would be required to practice the invention as claimed due to the amount of experimentation necessary because of the limited amount of guidance and limited number of working examples in the specification, the nature of the invention, the state of the prior art, breadth of the claims and the unpredictability of the art.

As set forth in *In re Fisher*, 427 F2.d 833, 839, 166 USPQ 18, 24 (CCPA) 1970: [Section 112] requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.

Claims 28-39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Although the claims are vague, indefinite, confusing and not logical, one interpretation of the claims may be that the container of the body fluid has an inner layer of a plastic which is not PVC, while an outer layer of material is made of PVC. This appears to be a novel type of blood bag or container, which is not described in the prior art. The specification is completely silent with regard to how such a container may be formed. For example, no technical elements for the formation of such a novel bag (container) are given. No dimensions of the total thickness of the walls, thickness of the layers, types of plastics which are compatible with each other and the body fluid to be stored, etc., are given. For example, when platelets are stored in plastic bags, the gas permeability or oxygen diffusion capacity of the bags is of import to the stability of the stored platelets, Wallvik *et al.* [V and D4]. The specification does not teach how to make this new type of container for containing body fluids. Thus, the specification is not enabled for this construction and is not enabled

for this element in the pending claims. Construction of a container suitable for "bodily fluids" such as blood cells, sperm and organs is an empirical art with many unknowns, the parameters of which appear to be distinct for the distinct stored elements.

*Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action: (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Because the claims are indefinite and open to many interpretations, the following rejection is made in the interest of compact prosecution.

Claims 28-39 are rejected under 35 U.S.C. § 103 as being unpatentable over Lambrecht *et al.* [B13] or Mohr [C13] in combination with Wallvik *et al.* [D4] or Rock *et al.* [V] and US Pat. 4726949 [B4] or US Pat. 5030200 [C10].

The claims are drawn to a method of viral inactivation comprising providing a body fluid in a first container and methylene blue in a second container both of which have an inner surface made of a non-polyvinyl chloride material, mixing the two and irradiating the mixture under "no-flow" conditions.

Mohr *et al.* disclose a method of virus inactivation comprising providing sterile plasma in a plastic blood bag and sterile methylene blue suitable for injection in an ampule, mixing the two in a blood bag and irradiating (Materials and Methods). This reference lacks the specific disclosure of the plastic blood bag having at least an inner surface made of a non-PVC material. The ampule is glass which is a non-PVC material.

Lambrecht *et al.* disclose a method of virus inactivation comprising providing sterile plasma in a plastic blood bag and sterile methylene blue in an ampule, mixing the two in the blood bag and irradiating the mixture (Materials and Methods). Although it is disclosed that the blood bags are obtained from Baxter or Biotest, the specific plastic from which they are constructed is not disclosed. However, the reference specifically discloses advantages to inactivating viruses in plasma by using methylene blue and irradiation "in their original containers" (p. 211).

Wallvik *et al.* [D4] disclose blood bags made of either PVC or polyolefin.

Rock *et al.* disclose blood bags made of polyolefin or PVC.

US 4,726,949 to Miripol *et al.* discloses the method of irradiating a blood component in a plastic bag under no flow conditions (col. 1, line 53, col. 4, l. 45).

US 5,030,200 to Judy *et al.* discloses the irradiation of a blood component and a photoactive agent under static conditions (col. 16, l. 61).

It would have been obvious to substitute any containers made of any material known in the art in the method of Mohr *et al.* or Lambrecht *et al.* where a blood bag obtained from Baxter is used because Wallvik *et al.* or Rock *et al.* each disclose a container made from polyolefin to store platelets or red cells, respectively. A polyolefin container has an inner surface which is not a PVC material.

It would have been obvious to add one component to the other in whatever art appropriate container and in whatever order one of skill in the art wished in the absence of evidence to the contrary regarding the criticality of such an addition or container.

It would have been obvious to irradiate the blood component and methylene blue in the method of Mohr *et al.* or Lambrecht *et al.* under no flow conditions because US 4,726,949 or US 5,030,200 disclose irradiation of blood components under no flow or static conditions. Also, both Mohr *et al.* and Lambrecht *et al.* irradiate the mixture of plasma and methylene blue in sealed blood bags which is the same system as disclosed in the present specification.

No flow of the mixture is disclosed by the primary references during irradiation.

It would have been obvious to use a non-PVC material to contain the methylene blue because both Mohr *et al.* and Lambrecht *et al.* disclose that the 1 ml sterile solution of 1% methylene blue which is suitable for i.v. use or intravenous use is sold by Neupharma in an ampule. Ampules are known by those of ordinary skill in the art to be glass, which is a non-PVC material. In the absence of criticality, one of skill in the art may use any container known in the art including polyolefin bags to contain an art related material.

One of skill in the art would have been motivated at the time of invention to make this substitution in order to obtain the results as suggested by the references with a reasonable expectation of success. The claimed subject matter fails to patentably distinguish over the state of the art as represented by the cited references. Therefore, the claims are properly rejected under 35 U.S.C. § 103.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1651. The supervisor for 1651 is M. Wityshyn, (703) 308-4743.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Saucier whose telephone number is (703) 308-1084. Status inquiries must be directed to the Customer Service Desk at (703) 308-0197. The number of the Fax Center for the faxing of papers is (703) 308-2742 or (703) 305-3592.

Sandra Saucier
Primary Examiner
Art Unit 1651
July 17, 2001